REMARKS

Reconsideration of this application is respectfully requested.

Claims 31-32 have been canceled without prejudice. New claims 33-38 have been added. Support for the new claims can be found, for instance, in pending claims 25-30 and in the specification at page 4, second full paragraph, and page 5, first full paragraph. No new matter is added by the amendments. Claims 25-30 and 33-38 are pending.

Claims 31-32 stand rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. Applicants respectfully submit that this rejection is now moot, in view of the present cancellation of claims 31 and 32. Withdrawal of the rejection is therefore respectfully requested.

Enablement Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 25-32 stand rejected as not being enabled. The Office contends that while the claims are enabled for *in vitro* activation of immune system cells against HIV, the claims are not enabled for *in vivo* activation. Applicants respectfully traverse the rejection.

The law on enablement, as clearly set forth by the Federal Circuit's predecessor court in In re Marzocchi, requires the Patent Office to provide specific reasons for a §112 rejection:

> As a matter of patent office practice...a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.
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> ...
>
> It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

In re Marzocchi, 439 F.2d 220, 223-224 (C.C.P.A. 1971) (emphasis in the original). Furthermore, the evidence or reasoning supplied by the Examiner must be particularized and definite, not broad and general:

> [W]e do not consider that a broad allegation that the application disclosure is speculative, coupled with a recitation of various difficulties which might be encountered in attempting to put it into practice, and a further assertion that there might still be other difficulties which would not be foreseen, constitutes a sufficiently definite statement of a basis for rejection.

In re Chilowsky, 229 F.2d 457, 462 (C.C.P.A. 1956).

The Office has focused its enablement rejection on the functional language contained in claim 25: "composition for *activation of immune system cells against HIV*...." It is respectfully submitted, however, that the present claims are not directed to a method of treatment, but are rather directed to

pharmaceutical compositions. The inquiry, therefore, is whether the specification enables the claimed compositions.

The specification contains a description of the manner and process of making the claimed invention. The claims are directed to a pharmaceutical composition comprising HIV infected cells that have been treated with hyaluronidase. See claim 1. The specification describes the formation of pharmaceutical compositions. See for instance page 5, 2nd and 3rd Full Paragraphs. The specification also provides a detailed description of how to treat HIV infected cells with hyaluronidase, of which the claimed compositions are comprised. See for instance, page 12, Study 2, and page 14, Study 4. Clearly, therefore, the specification teaches how to make the claimed composition.

The specification also discloses how to use the claimed compositions. For instance, techniques of administration and dosage regimens are described at page 5, last paragraph, to page 6, third full paragraph. Since the specification contains a teaching of the manner and process of making and using the claimed compositions, the enablement requirements of § 112, first paragraph, are met. Withdrawal of the § 112 rejection of claims 25-32 is therefore respectfully requested.

As discussed above, the Office has focused the enablement analysis on the functional language in the claims, rather than

on whether the compositions that are actually claimed are enabled. Notwithstanding, Applicants respectfully submit that the Office has not met its burden of supporting its position with acceptable evidence or reasoning.

The evidence cited by the Office does not support the enablement rejection. The Office cites Fresheny (Culture of Animal Cells, a Manual of Basic Technique, Alan R. Liss, Inc., 1983, page 4) as indicating that there are many differences between *in vitro* cultured cells and their *in vivo* counterparts. However, Fresheny's observations are general in nature, and are not specific to Applicant's assays. In addition, despite the observed differences between cell environments, Fresheny still directs that "it must be emphasized that many specialized functions are expressed in culture and as long as the limits of the model are appreciated, it can become a very valuable tool." Fresheny, therefore, does not cast doubt on Applicants' invention.

Indeed, Fresheny is not reliable evidence. Fresheny was published in 1983. Fresheny therefore predates Applicants' filing date by about 19 years! The state of the art in 1983 cannot be considered to be indicative of the state of the art in 2002, especially in a rapidly progressing field such as biology. Fresheny, therefore, cannot be considered reliable evidence.

Applicants wish to draw the Office's attention to the factual situation in Burroughs Wellcome Co. v. Barr Laboratories, Inc., 40 F.3d 1223 (Fed. Cir. 1994). Burroughs Wellcome involved a series of patents covering various preparations and methods of using azidothymidine (AZT) in the treatment of persons infected with HIV. Id. at 1224. Burroughs Wellcome screened the AZT compounds, claimed in its patents, for antiretroviral activity using two murine (mouse) retroviruses. Id. at 1225. The alleged infringers argued that conception of the Burrough's Wellcome's claimed invention did not occur until the operability of the invention had been confirmed using an NIH assay which utilized a line of T-cell clones based on the ATH8 cell line. Id. at 1227. The court did not agree with the alleged infringers, ruling instead in favor of the patentees. Id. at 1228.

As noted by the court, enablement and conception are distinct issues, and one need not necessarily meet the enablement standard to prove conception. Id. at 1231. Nevertheless, the court concluded "the enabling disclosure does suffice in this case to confirm that the inventors had concluded the mental part of the invention process [conception of the invention]...." Id. The court, therefore, implicitly believed that the inventors' murine assays were sufficient for an enabling disclosure.

Applicants' studies utilize human cell lines and HIV, and not a murine virus, as in the Burroughs Wellcome Co. case. Applicants' submit that if the Federal Circuit considers a murine assay to sufficiently enable an HIV drug, then Applicants' assays, which use human cell lines and the HIV virus, are also enabling.

Finally, Applicants draw the Office's attention to the enclosed printout from the National Institutes of Health (NIH) website. The printout describes the NIH's *in vitro* anti-HIV screens for the evaluation of chemical libraries. Use of such in vitro assays by the NIH for anti-HIV screening, which are analogous to Applicants' assays, supports Applicants' position that the in vitro assays in the application would be understood by a person of ordinary skill in the art to correlate with in vivo activity.

For at least the reasons discussed above, the claims are fully enabled by the specification. Accordingly, withdrawal of the § 112 rejection is respectfully requested.

New Claims 33-38 are Allowable

Applicants respectfully submit that new claims 33-38 are allowable. The new claims are directed to compositions comprising HIV infected cells that have been treated with hyaluronidase. While Applicants do not agree with the Office's non-enablement rejection, as discussed above, the new claims do

not contain the language concerning activation of immune system cells against HIV. Applicants submit that these claims are allowable. Notice to this effect is respectfully requested.

Allowance of all the pending claims and passage of the case to issue are respectfully solicited. Should the Examiner believe a discussion of this matter would be helpful, the Examiner is invited to telephone the undersigned at (312) 913-0001.

Respectfully submitted,

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Developmental Therapeutics Program NCI/NIH
http://dtp.nci.nih.gov/docs/aids/anti-hiv-screening.html
Discovery Services
Screening Services In Vitro Anti-HIV Screen

The anti-human immunodeficieny virus (HIV) assay is a relatively simple method to determine the ability of a drug to protect cells against the cytopathic effects of HIV. T-lymphocyte-derived CEM cells are added to 96-well microtiter plates along with cell-free HIV and the test agent at 1/2-log dilutions over a multi-dose range. Six days after infection, a tetrazolium reagent, XTT, is added to the wells. In the presence of viable cells, XTT is metabolized to an orange colored formazan, such that the quantity of viable cells, and thus, the protective ability of the test agent, is proportional to the depth of the color. Uninfected cells are also treated with drug in order to determine the cytotoxicity of the drug, if any, to the CEM cells. Screening data and chemical structures for more than 40,000 compounds is available.

Input to this assay is approximately 2,500 to 3,000 compounds per year. The submission of single pure compounds to this screen is via the on-line submission form, and requires that the compound structure be novel and be accompanied by a biologic rationale.

The high throughput version of the assay was developed to allow the evaluation of chemical libraries. It is performed in 384-well plates at a single high dose, and does not include an addition of test agent to uninfected cells. Researchers interested in submitting libraries to this assay should contact:

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